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SHORT COMMUNICATION

Paracetamol orodispersible tablets: a risk for severe poisoning in children?

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Abstract
Purpose Childhood paracetamol (acetaminophen) ingestion with subsequent risk of hepatotoxicity is a major medical problem. The aim of this study was to investigate the risk of high-dose ingestion of orodispersible, fast-disintegrating paracetamol tablets in children.
Methods A retrospective single-center case study of all accidental selfadministrations of solid or orodispersible 500-mg paracetamol tablets occurring in children ≤6 years, reported to the Swiss Toxicological Information Centre between June 2003 and August 2009.
Results We found 187 cases with ingestion of solid 500-mg paracetamol tablets and 16 cases with ingestion of orodispersible 500-mg tablets. The mean ingested dose in the orodispersible-tablet group was 59% higher than in the solid-tablet group (p=0.085). Administration of activated charcoal and/or N-acetylcysteine because of ingestion of a potentially hepatotoxic paracetamol dose (≥150 mg/kg body weight) was recommended in 32 patients (17.1%) in the solid-tablet group and in five (31%) in the orodispersible-tablet group.
Conclusions Orodispersible paracetamol formulations may represent an important risk factor for severe paracetamol poisoning in children. Over-the-counter availability may contribute to increasing the use of this galenic formulation and eventually the number of poisonings in children.

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Introduction

Childhood paracetamol (acetaminophen) ingestion with the inherent risk of hepatotoxicity is a major medical problem in most parts of the world. The issue of over-the-counter medications leading to unintentional ingestions in children and the importance of child-resistant closures for liquid paracetamol preparations has already been addressed in previous studies [1, 2]. At the beginning of 2002, an over-the-counter orodispersible paracetamol formulation was licensed in Switzerland. The aim of this study was to investigate the risk of high-dose ingestion of orodispersible, fast-disintegrating paracetamol tablets in children.

Methods

Data acquisition and inclusion criteria

The Swiss Toxicological Information Centre (STIC) collects specific information from laypersons and detailed clinical reports from physicians and hospitals about poisoning cases by means of an in-house computer-based and structured data recording and analysis system [3]. At the time of the initial phonecall, clinical information is obtained, such as the patient's age and gender, circumstances of intoxication, ingested doses of all substances involved, symptoms, and causality. These data are verified and supplemented by information from discharge letters and laboratory reports where available. We performed a retrospective single-center analysis of all cases reported to

Table 1 Comparison of cases with solid versus orodispersible paracetamol tablets ingestion

	Solid paracetamol $n=187$	Orodispersible paracetamol $n=16$	P value
Age (years): mean ± SD, (range), median	2.3±0.92 (0.8–6), 2	3±1.21 (1.5–5), 2.5	0.046
Number of ingested tablets: mean ± SD, (range), median	2.5±1.96 (0.3–8), 2	4.6±3.76 (1–14), 4	0.057
Ingested dose in mg/kg: mean ± SD, (range), median	98.7±77.7 (8.3–444), 71	157.3±147.6 (29.4–538), 100	0.085

our center of accidental self-administration of solid or orodispersible 500-mg paracetamol tablets occurring in children ≤6 years during the period June 2003 through August 2009. Only cases with acute ingestion of a single substance (paracetamol) and available information on the ingested dose were included.

Statistical evaluation

Statistical analysis was performed with SPSS software (Version 17.0; SPSS Inc., Chicago, IL, USA). Between-group comparisons were made using the Mann–Whitney U test (two-tailed).

Results

A search of our database yielded 187 pediatric cases with ingestion of solid 500-mg paracetamol tablets (group 1) and 16 pediatric cases with ingestion of orodispersible 500-mg tablets (group 2) which fulfilled the inclusion criteria. A comparison of the two groups in terms of patient age, number of ingested tablets, and ingested dose is shown in Table 1. The mean ingested dose in the orodispersible-tablet group was 59% higher than in the solid-tablet group, although the difference did not reach statistical significance ($p=0.085$). In nine patients (4.8%) in the solid-tablet group and one (6.25%) in the orodispersible-tablet group, primary gastrointestinal decontamination with orally administered activated charcoal was recommended, because paracetamol intake was between 150 and 200 mg/kg body weight. In 23 patients (12.3%) in the solid-tablet group and four (25%) in the orodispersible-tablet group, hospitalization for N-acetylcysteine (NAC) treatment was recommended because paracetamol intake was ≥200 mg/kg body weight. Overall, oral administration of activated charcoal and/or NAC because of ingestion of a potentially hepatotoxic paracetamol dose was recommended in 32 patients (17.1%) in the solid-tablet group and in five (31%) in the orodispersible-tablet group. Analysis of the clinical course of paracetamol-poisoned children was not the focus of this study. However, among the cases where such information was available, no symptoms or signs of hepatotoxicity were observed after appropriate treatment, and patients remained asymptomatic, except for two among those hospitalized for NAC administration who showed mild gastrointestinal symptoms such as nausea and vomiting (one in the orodispersible-tablet group and one in the solid-tablet group).

Discussion

Possible factors leading to ingestion of higher paracetamol doses with the orodispersible formulations are rapid disintegration of the tablets within seconds of contact with saliva, the pleasant feeling in the mouth, the masked bitter paracetamol taste, and the candy-like aspect, which may encourage consumption by children [4]. Further factors not directly associated with the orodispersible formulation, such as lack of child-resistant closure and blister safety packaging, lack of vigilance by parents and caregivers in the storage of medications, and availability of adult-strength tablets, may have acted as confounders that we were unable to control for in analyses and which possibly contributed to increasing the risk of high-dose paracetamol ingestion in the orodispersible-formulation group.

Study limitations

The interpretation of our findings is limited by the retrospective nature of the study design. In addition, data from poison control centers are subject to reporting bias, as we do not know the percentage of cases reported to the STIC. Furthermore, the decision to only include patients who ingested paracetamol alone led to small case numbers.

Conclusions

This study highlighted the problem of the availability of orodispersible paracetamol formulations, which may represent an important risk factor for severe paracetamol poisoning in children. Over-the-counter availability may contribute to increasing the use of this galenic formulation and eventually the number of poisonings in children. Further studies with larger case numbers are required to confirm our findings.

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Conflict of interest None

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